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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) 03715.0110-00000	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on _____ Signature _____ Typed or printed name _____		Application Number 10/069,405	Filed May 29, 2002
		First Named Inventor Jean-Pierre Benoit	
		Art Unit 1794	Examiner TRAN, Thao. T.
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p> <p>I am the</p> <p><input type="checkbox"/> applicant/inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.</p> <p><input type="checkbox"/> attorney or agent of record. Registration number _____</p> <p><input checked="" type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 <u>48,638</u></p> <p>Date <u>April 2, 2007</u></p> <p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p>			
<p><input checked="" type="checkbox"/> *Total of 1 form is submitted.</p>			

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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I. Status of the claims

Claims 1, 3-21, and 25-41 are pending claims in this application and have been at least twice rejected. In response to the Office Action dated January 4, 2008, ("Office Action"), Applicants respectfully request a *second* pre-appeal brief review of the outstanding rejections.¹

II. Claim rejections under 35 U.S.C. § 103(a)

The Office rejected claims 1, 3-21, and 35-41 under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 95/13799.

The Office argues that WO 95/13799 teaches "a process for microencapsulating an active agent by coacervation, the process consisting of dissolving a polymer in an organic solvent, which contains the active substance; mixing the polymer/active agent solution (first phase) with another liquid (second phase) to form microdroplets of the active agent encapsulated in the polymer; quenching the mixture at 0-4°C with water or an aqueous solution." Office Action at 2. Applicants respectfully traverse this rejection.

A. The disclosure in WO 95/13799

The Office cites to Figures 1-3; p. 9, ¶ 3; and p. 15, ¶¶ 2-3 of WO 95/13799 as forming the basis of the instant obviousness rejection. Office Action at 2. The figures and the passages show a method comprising:

- 1) preparing a first phase comprising a polymer and an active ingredient dissolved or dispersed in a solvent blend (mutually miscible solvents; *i.e.*, a single phase) (p. 9; *see also* bottom of p. 13). The solvent blend may comprise "at least two of the following: an ester, an alcohol, and a ketone" (p.15);

¹ The first pre-appeal brief review was requested on Nov. 21, 2006. In response, the Office withdrew the outstanding rejections and reopened prosecution.

- 2) preparing a second phase comprising an aqueous solution, *which is immiscible with the first phase* (p. 9; *see also* the "Summary of Invention" at p. 8, lines 10-11);
- 3) combining the first and second phases (p. 9); and
- 4) isolating the microparticles formed in step (3) (p. 9).

B. The Office's arguments in support of the rejection

The Office acknowledges that WO 95/13799 "teaches adding a mixture of ethyl acetate and an alcohol or ketone, instead of adding ethyl acetate first and then the alcohol or ketone." *Id.* at 3. However, the Office attempts to remedy this deficiency in WO 95/13799 by arguing that "adding a mixture of ingredients has been held *prima facie* obvious over adding them sequentially since they would have given substantially the same results." *Id.*

The Office seems to argue that there would not be any difference in the end result if both components of the solvent blend used in WO 95/13799 are used together in a single step, or added in separate steps. The Office argues that one of the two solvents required in WO 95/13799's solvent blend (such as ethyl acetate) can serve to dissolve the polymer and that the second component of the blend, such as "an alcohol or a ketone of 1 to 3 carbon atoms, which includes ethanol and propanol, meet[s] the requirement of the non-solvent in claims 1 and 41." Office Action at 3. However, as will be shown below, regardless of whether the components of the solvent blend are added together or in separate steps, WO 95/13799 does not disclose any solvent that can be a component of WO 95/13799's solvent blend and also meet the requirements of the instantly recited non-solvent.

The Office then relies on inherency by arguing that "[i]t is noted that since WO '799 uses the same organic solvent, non-solvent, and curing agent as presently claimed, the composition of the reference would inherently have the same properties and characteristics,

such a dissolution or miscibility as the claimed invention." *Id.* However, because WO 95/13799 does not use the same components, nor perform the same steps, as presently claimed, the results cannot be inherent.

C. The Office's has not used the proper standard for obviousness

Throughout prosecution, the Office seemed more concerned with finding equivalents in WO 95/13799 for Applicants' solvents, non-solvents, and curing agents, than with explaining how one of ordinary skill in the art would have modified the *methods* taught in WO 95/13799 to meet the claimed method steps.

The Office has failed to analyze the *Graham* factors as required by the M.P.E.P. See, e.g., M.P.E.P. § 2141.I. For example, the Office has failed to indicate the difference between the method steps taught in WO 95/13799 and the instant invention and how one of ordinary skill in the art would have modified such steps to arrive at the instant invention.

Most notably, Applicants point out that step 2 described above in the method of WO 95/13799 requires that "said first phase is substantially immiscible in said second phase." WO 95/13799 at 10, lines 23-24. In contrast, the non-solvent of the invention "is miscible with said organic solvent for the polymer." Instant claim 1. That is, the method of WO 95/13799 results in the formation of two liquid phases, whereas in the instant method, the mixing of the solvent for the polymer and the non-solvent results in a single liquid phase. The Office has not acknowledged this difference, nor has it explained how one of ordinary skill in the art could have bridged this gap to arrive at the instant invention. Applicants incorporate herein by reference Annex A (enclosed with the response filed on October 25, 2007), which schematically explains differences between the instant invention and WO 95/13799. For at least the foregoing reason, the Office has not made a *prima facie* case of obviousness, and Applicants respectfully request that this rejection be withdrawn.

D. The modifications suggested by the Office do not produce the claimed invention

As a preliminary matter, Applicants point out that the Office's proposed modification of separating the blend of solvents and using the components in two separate steps is contrary to the teachings in WO 95/13799. The reference states that "[t]he solvent system used herein *is a blend of at least two solvents.*" WO 95/13799 at 13, line 28 (italics added).

However, even if one of ordinary skill in the art ignored this requirement and split the use of the solvent blend into two separate steps, the result would not be instant invention. As mentioned in section II.B above, the Office seems to suggest that one component of WO 95/13799's solvent blend can act as an "organic solvent" and the other component of the same solvent blend act as a "non-solvent." However, the Office is ignoring that WO 95/13799 states that *each component* of the solvent blend "must be . . . capable, when blended, of dissolving polymeric matrix material." WO 95/13799 at paragraph bridging 13-14. Thus, it is clear the same solvent cannot dissolve the polymer, as required by WO 95/13799, and at the same time perform the functions of the instantly recited "non-solvent," which is not a solvent for the polymer. See Claim 1. The Office has not explained why one of ordinary skill in the art would have ignored the teachings in WO 95/13799 regarding the properties of each solvent in the solvent blend.

E. The Office's reliance on inherency is misplaced

The Office argues that since "the same chemicals are used in [WO 95/13799], the composition of [WO 95/13799] would inherently have the same properties." Office Action at 5. However, as mentioned above, the same chemicals cannot be used in WO 95/13799 and in the instant invention because WO 95/13799 requires that all of the components from the solvent blend dissolve the polymer.

Therefore, no component from the solvent blend can act as the non-solvent of the present invention. For at least this reason, the Office reliance on inherency is inapposite. Moreover, Applicants respectfully remind the Office that inherency arguments are not appropriate in an obviousness analysis. M.P.E.P. § 2141.02.V (explaining that "[o]bviousness cannot be predicated on what is not known at the time an invention was made, even if the inherency of a certain feature is later established.")

If, on the other hand, the Office argues that the second phase in WO 95/13799 corresponds to Applicants' non-solvent, then such second phase, which is immiscible with the first phase (WO 95/13799 at 10, lines 23-24), fails to meet the instant limitation wherein the non-solvent "is miscible with said organic solvent [*i.e.*, WO 95/13799's first phase.]"

Moreover, the results of the method steps recited in WO 95/13799 are significantly different from those in claim 1. For example, in the claimed invention, deposition of the polymer on the surface of the active principle occurs after addition of the non-solvent to the polymer solution. *See, e.g.*, claim 1. This limitation is not met by the modifications to WO 95/13799 suggested by the Office, where the addition of the second immiscible aqueous phase to the first organic phase does not result in deposition of the polymer on the surface of the active principle. *See, e.g.*, WO 95/13799 at paragraph bridging 25-26; Examples 1-3. Solid microparticles do not form in WO 95/13799 *until after* the emulsion of organic solvent/aqueous solution is quenched with a quench liquid. *Id.*

It is clear, therefore, that the two processes operate under different principles and that the claimed invention would not result from an optimization of the process disclosed in WO 95/13799, as alleged by the Office. Accordingly, Applicants respectfully request that this rejection be withdrawn.